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EXAMINER	
CANELLA, KAREN A	
ART UNIT	**PAPER NUMBER**
1642	6

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/756,398	Le et al
Examiner	**Art Unit**
Karen Canella	1642

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3 months* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☐ Responsive to communication(s) filed on _____ .

2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under ***Ex parte Quayle***, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-23* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1-23* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☒ Notice of References Cited (PTO-892)
16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
18) ☐ Interview Summary (PTO-413) Paper No(s). _____
19) ☐ Notice of Informal Patent Application (PTO-152)
20) ☐ Other:

DETAILED ACTION

1. Claims 1-23 are pending and examined on the merits.

Priority

2. This application claims to be a divisional of 09/133,119. However, no restriction of claims ever occurred in the '119 application and the instant specification is not a duplicate of the '119 specification. Amendment of the specification to recite the proper relationship of the instant application to 09/133,119 is required.

Information Disclosure Statement

3. The infomation disclosure statment submitted on July 9, 2001 has been considered. However, a 1449 Form was not included with a list of the pertinent references, therefore the examiner cannot make of record the exact references which were submitted..

Claim Rejections - 35 USC § 102

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

5. Claim 3 is rejected under 35 U.S.C. 102(b) as being anticipated by either of Hardmann et al (EP-323806, 1989) or Jarvis et al (J Immunol, 1989, Vol. 143, pp. 4213-4220). Claim 3 is drawn to isolated nucleic acids that hybridizes under conditions of moderate stringency to the complements of SEQ ID NO:2 or SEQ ID NO:4, wherein the nucleic acid are expressed with SEQ ID NO:4 or SEQ ID NO:2, respectively and a gene encoding for an immunoglobulin constant region encode a polypeptide which binds to TNF alpha. Hardmann et al disclose an isolated nucleic acid of a light chain murine variable region which would hybridize under

conditions of moderate stringency to he complement of SEQ ID NO:2; Jarvis et al disclose an isolated nucleic acid of a heavy chain murine variable region which would hybridize under conditions of moderate stringency to he complement of SEQ ID NO:4. As the prior art nucleic acids are similar in sequence and encode the light and heavy chain regions of murine antibodies, it is reasonable to conclude that when said prior art nucleic acids are expressed with corresponding light chain variable region or heavy chain variable region of the instant invention in addition to an IgG1 immunoglobulin region, that the prior art nucleic acids would encode a polypeptide which binds to human TNF-alpha.

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

7. Claims 1-23 are rejected under 35 U.S.C. 103(a) as being unpatentable over any of Rathjen et al (US 5,959,087) or Yone et al (US 5,075,236) or Moeller et al (US 5,231,024) or

Hirai et al (J or Immunological Methods, 1987, Vol. 96, pp. 57-62) or Fendly et al (Hybridoma, 1987, Vol. 6, pp. 359-370) or Meager et al (Hybridoma, 1987, Vol. 6, pp. 305-310) or Liang et al (Biochemcal and biophysical Research Communications, 1986, Vol. 137, pp. 847-854) or Bringman et al (Hybridoma, 1987, vol. 6, pp. 489-507) or Exley et al (Lancet, 1990, Vol. 335, pp. 1275-1277) or Yan et al (Chinese Journal of biotechnology, 1991, Vol. 7, pp. 121-126) all in view of Cabilly et al (US 4,816,567). Claims 1, 2, 3, 5, 6, 13-20 are drawn to isolated nucleic acids which hybridize under highly stringent or moderately stringent conditions to the complements SEQ ID NO: 2 or SEQ ID NO:, wherein said nucleic acids when expressed with the polynucleotide encoding the corresponding heavy or light chain variable region, as set forth in SEQ ID NO:2 and SEQ ID NO:4 along with a gene encoding a IgG1 immunoglobulin region, encode a protein which binds TNF. Claims 18-20 specify that the encoded polypeptide binds and inhibits THF alpha. Claims 4 and 21 are drawn to an isolated nucleic acid which when expressed with a polypeptide comprising SEQ ID NO:5 or SEQ ID NO:3 and an IgG1 immunoglobulin constant region, encodes a polypeptide comprising SEQ ID NO:3 or SEQ ID NO:5, which binds TNF. Claim 21 specifies that the encoded polypeptide both binds and inhibits THF ALPHA. Claims 5, 6, 22 and 23 are also drawn to SEQ ID NO:2, the complementary strand of SEQ ID NO:2; SEQ ID NO:4 and the complementary strand of SEQ ID NO:4. Claims 7-12 specifically embody expression vectors comprising the claimed isolated nucleic acids.

Any of Rathjen et al or Yone et al or Moeller et al or Hirai et al or Fendly et al or Meager et al or Liang et al or Bringman et al or Exley et al or Yan et al teach neutralizing antibodies to human TNF alpha. Rathjen et al teach Mab 1 which binds to residues 58-65 of human TNF and Mab 57 which binds to residues 56-79 of human THF ALPHA(column 18, line 60, column 19, line 4), thus overlapping with the instant antibodies which bind to residues 59-80 and 87-108 of human TNF alpha, thus overlapping with the A2 antibody of the instant specification which binds to epitopes within residues 59-80 and 87-108 of human TNF alpha. Yone et al teach neutralizing anti-TNF alpha antibodies which bind to epitopes contained in the 68th to the 97th residues of

human TNF alpha. Moeller et al teach AM-114 and AM-195 antibodies which neutralize human TNF alpha. Hirai et al teach the monoclonal antibody 3B10 which neutralizes human TNF-alpha. Fendly et al teach the monoclonal antibodies 226-7F4, 241-1H11, 245-10E11, 245-15C8 which neutralize human TNF-alpha. Yan et al teach the monoclonal antibodies of B5, Z8, Z12, and Z20 which can neutralize human TNF alpha. .None of the prior art reference teach the isolated nucleic acids encoding the disclosed antibodies, nor an expression vector comprising said isolated nucleic acids.

Cabilly et al teach the isolation of mRNA encoding recombinant antibodies and the transfer of the polynucleotide into an expression vector.

It would have been *prima facia* obvious to one of ordinary skill in the art at the time the claimed invention was made to isolate the polynucleotides encoding the prior art antibodies and clone it into expression vectors.

One of ordinary skill in the art would have been motivated to do so with a reasonable expectation of success by the teachings of Cabilly et al on superiority of cloning nucleic acids encoding monoclonal antibodies into vectors for the recombinant expression of said antibodies, and the further teachings of Cabilly et al on the improvements in purity, stability, flexibility and economy afford by such recombinant method (column 2, lines 40-68). Further although the references do not specifically teach that the prior art antibodies are encoded by nucleotides which comprise SEQ ID NO:4, or SEQ ID NO:2, or hybridize under stringent or moderately stringent conditions to the complements of SEQ ID NO:2 or SEQ ID NO:4 , it appears that the prior art monoclonal antibodies are the same as the instant monoclonal antibodies. The office does not have the facilities and resources to provide the factual evidence needed in order to establish that the product of the prior art does not possess the same material, structural and functional characteristics of the claimed product. In the absence of evidence to the contrary, the burden is on the applicant to prove that the claimed product is different from those taught by the prior art.

See In re Best 562F.2d 1252, 195 USPQ 430 (CCPA 1977) and Ex parte Gray 10 USPQ 2d 1922 (PTO Bd. Pat. App. & Int. 1989).

Double Patenting

8. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

9. Claims 10-23 are rejected under the judicially created doctrine of double patenting over claims 1-4 of U. S. Patent No. 6,277,969 since the claims, if allowed, would improperly extend the "right to exclude" already granted in the patent.

The subject matter claimed in the instant application is fully disclosed in the patent and is covered by the patent since the patent and the application are claiming common subject matter, as follows: the nucleic acids comprising SEQ ID NO:2 and SEQ ID NO:4 and expression vectors thereof; nucleic acids encoding SEQ ID NO:3 and SEQ ID NO:5 and expression vectors thereof.

Conclusion

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Karen Canella whose telephone number is (703) 308-8362. The examiner can normally be reached on Monday through Friday from 8:30 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa, can be reached on (703) 308-3995. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Karen A. Canella, Ph.D.

Patent Examiner, Group 1642

March 25, 2002

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